Relative Bioavailability of Dioxin/Furan Mixtures in Soils[1] (Ingestion Pathway)

Issue

Ecology is considering establishing a default gastrointestinal absorption fraction[2] for dioxin/furan mixtures equal to 0.4 that would be used when establishing soil cleanup levels. Based on available data is this default value scientifically defensible?

Background

The Model Toxics Control Act (MTCA) Cleanup Regulation provides methods to establish residential (unrestricted land use) and industrial (restricted land use) soil cleanup levels (WAC 173-340-740 through -745). The gastrointestinal (GI) absorption fraction is one of several factors considered when establishing soil cleanup levels. The MTCA rule establishes a default GI absorption fraction of 1.0 which applies to most chemicals including dioxins and furans. This value is based on the assumption that soil-bound hazardous substances are absorbed to the same extent as hazardous substances administered in the studies used to establish the cancer slope factor and/or reference dose.

Ecology is proposing to revise WAC 173-340-740 and -745 to establish a default GI absorption factor of 0.4 that would be used when establishing soil cleanup levels for dioxin/furan mixtures. The current default GI absorption value of 1.0 would continue to be applied for other hazardous substances. Method B soil cleanup levels for dioxins/furans would be established at a soil concentration of 17 ppt. Industrial soil cleanup levels would be established at a soil concentration of 2,200 ppt. Ecology's rationale for the proposed revisions includes:

- Approach has a strong underlying scientific basis (soil matrix effect).
- The proposed default value falls within the range of experimental results.
- The proposed default value is consistent with EPA Dioxin Reassessment.
- The approach is consistent with several expert committee findings.
- The approach is consistent with approaches being used by some state environmental agencies.

The Board reviewed this question and reached several conclusions at the October 23rd meeting:

- Based on available scientific information, it is reasonable to conclude that soil-bound dioxins and furans are less bioavailable than dioxins and furans in foods and drinking water.

[1] Ecology's review of this issue is focused on the procedures for establishing soil cleanup levels based on soil ingestion and cancer risk. Ecology does not believe that similar adjustments are necessary for other exposure pathways (e.g. food/water ingestion and inhalation). At this point, Ecology is uncertain whether a similar adjustment would be appropriate when evaluating non-cancer risks resulting from soil ingestion and dermal contact.

[2] WAC 173-340-200 defines "Gastrointestinal absorption fraction" as "... the fraction of a substance transported across the gastrointestinal lining and taken up systematically into the body...".

- It is important to consider the absorption of dioxins and furans in soils relative to the amount of absorption in the toxicological studies that were used to establish the cancer slope factors and reference doses.
- Based on available scientific information, it is reasonable to assume that test animals absorbed 80% of the administered dose in the toxicological study used to establish the cancer slope factor for dioxins and furans (Kociba et al. 1978)

However, the Board did not reach a conclusion on whether it was reasonable to use a 30% absorption value for soil-bound dioxins and furans. They requested that Ecology provided additional information on the designs of key studies (e.g. soil types, test methods, etc.), the range of soil types at Washington cleanup sites and the range of factors that might influence inter- or intra-individual variability in absorption rates.

Summary and Review of Available Studies

Ecology worked with the Washington State Department of Health (Health) to review numerous studies on the absorption and bioavailability of mixtures of dioxins and furans. Ecology and Health identified six key studies that investigated the absorption of soil-bound dioxins and furans. Information from these six studies is summarized in the tables at the end of this discussion paper. Key observations include:

- In total, the 6 studies evaluated oral absorption of dioxins from soil collected at 5 sites. Experimental protocols, animal species, and measured endpoints varied among the studies.
- The studies focused on oral bioavailability of TCDD from soil. Little information about other congeners in soil has been published. Data from the studies suggest that bioavailability could range from < 1% to approximately 100% (refer to tables end of Issue Paper).
- Absorption of TCDD (dioxins/furans) from contaminated soils may be influenced by soil type (% carbon content), duration of contact with the soil, and different soil characteristics.
- Absorption and distribution of TCDD from soil appears to be dose specific and species specific. Studies of dioxins/furans administered orally in other media (e.g., food or oil) suggest that absorption and distribution may also be congener-specific.
- Depending on how absorption efficiencies were measured, (i.e., liver tissue concentrations, enzyme inductions, blood serum levels, etc), calculated bioavailability varied across different studies and within the same study using similar / same soils.
- Selection of specific per cent absorption efficiency for mixtures of dioxins/furans within the available ranges is a science-policy decision.

Review of Scientific Studies Using MTCA Quality of Information Criteria

Ecology considers a wide range of factors when developing revisions to the MTCA Cleanup Regulation (e.g. available scientific information, regulatory consistency, level of protection, implementation costs and benefits, etc.). The MTCA Cleanup Regulation establishes several procedural and substantive requirements to guide the evaluation of new scientific information when establishing site-specific cleanup requirements (WAC 173-340-702(16)). Although these criteria were established for site-specific determinations, Ecology believes that they provide a useful framework for evaluating the different types of scientific information considered during the rulemaking process. Ecology's review of the six quality of information criteria is summarized below.

- ***Whether the information is based on a theory or technique that has widespread acceptance within the relevant scientific community.....***

  There appears to be widespread agreement among risk assessors that the physical-chemical properties of a contaminant in combination with soil types and soil particle characteristics can influence the bioavailability of a soil contaminant:

  - The Institute of Medicine of the National Academies noted that the bioavailability of dioxin-like compounds from the soil reservoir varies from 20 to 40% (NAS, 2003, p. 76).
  - EPA (2003) concluded that soil-bound dioxins and furans are generally less bioavailable that dioxins and furans in food and drinking water.
  - The National Research Council (NRC, 2003) reviewed the available information on the bioavailability of contaminants in soils and sediments. They concluded that an assumption of 100% relative bioavailability is generally conservative because most toxicity tests use forms of a chemical that tend to be readily absorbed. However, they also observed that this is not always the case and that toxicity study conditions may represent sub-optimal conditions for absorption (p. 7).
  - Van den Berg et al. (2006) discussed the issue of bioavailability of soil-bound dioxin-like compounds within the context of using WHO TEF values. They concluded that "….the issue of matrix-specific bioavailability of these chemicals from abiotic environmental samples leads to a high degree of uncertainty for risk assessment as this is largely dependent upon the organic content and age of the particles. For example, direct application of these WHO TEFs for assessment of OCDD or OCDF present in soil, sediment or fly ash would lead to inaccurate assessment of the potential toxicity of the matrix. This derives primarily from the fact that the highly hydrophobic PCDDs and PCDFs bind strongly to particles thereby reducing their bioavailability for living organisms….As result, application of these WHO TEFs for calculating the TEQ for e.g. OCDD and OCDF in abiotic environmental matrices has limited toxicological relevance and use for risk assessment unless the aspect of reduced bioavailability is taken into consideration…." (p. 28)

- ***Whether the information was derived using standard testing methods or other widely accepted scientific methods.***

  The peer reviewed studies that Ecology has evaluated appear to use reasonable scientific principles and methods to evaluate soil bioavailability. However, there are currently no standard testing methods or a single testing method that has widespread use or acceptance within the scientific community. Indeed, the

National Research Council (NRC, 2003) stated that the tool box of methods for understanding the bioavailability processes in soils is incomplete.

The 6 peer reviewed bioavailability studies evaluated by Ecology have followed generally acceptable protocols with some studies (e.g., Lucier study) providing more detailed information with results that appear more dependable. No specific methodology has emerged from the literature reviewed that defines one methodology being superior over another or the most acceptable methodological approach within the scientific community. Please refer to the discussion regarding quality assurance/quality control procedures for some of the limitations associated with the bioavailability studies evaluated by Ecology.

- ***Whether a review of relevant scientific information, both in support of and not in support of the proposed modification, has been provided along with the rationale explaining the reasons for the proposed modification.***

Ecology recognizes that the reported oral bioavailabilities from soil for dioxins/furans have a very large range (< 1% to 100%). In the absence of a clear scientific direction that indicates a particular absorption efficiency, Ecology believes that the selection of one absorption efficiency over that of another is largely a science-policy decision.

Ecology has examined the available bioavailability studies in more detail. Calculation of the average and median relative bioavailability from these studies is shown in Table 1 (additional information is provided in the table at the end of this paper). Note that three different end points (all a reflection of liver concentration and liver enzyme activity) were used in the various studies--liver content/concentration, AHH induction and P450 induction. Table 1 shows the overall average and median bioavailability and the bioavailability based on these different end points. Ecology believes that the most reliable end point for this evaluation is the liver content since the enzyme induction will proceed from the liver concentrations. Although there is some congener-specific variation, the distribution of dioxins/furans in the body is determined by: metabolism, lipophilicity, and hepatic sequestration. The third determinant of the pharmacokinetic behavior of dixoins/furans is hepatic binding due to the dose-dependents induction of a hepatic binding protein. The induction of this liver protein is under the control of the Ah receptor and is dose and congener dependent (Schecter and Gasiewicz, 2003). For the 19 studies conducted using the liver end point, the average bioavailability was 46% and the median bioavailability was 52%. These values are close to the 40% derived from the EPA dioxin reassessment and proposed for this rule amendment.

Table 1: Summary of Dioxin Bioavailability Studies

End Point	All Studies	Liver Content	AHH Induction	P450 Induction
# of Studies	39	19	12	8
Range	0.25-121	0.25-71	49-121	65-117
Average	66	46	84	87
Median	65	52	87	87

Support For Ecology's Proposed Rule Change - Bioavailability

→ The proposed approach has a sound conceptual basis.

→ The revised default value falls within range of study results.

→ The proposed approach is consistent with the EPA dioxin reassessment evaluation and report.

→ The revised default value produces exposure estimates that represent reasonable maximum exposure values when used with other exposure parameters specified in the MTCA Cleanup Regulation.

Not in Support Of Ecology's Proposed Rule Change

→ Ecology's proposal fails to account for intra-individual variability (total body burdens, dietary habits & fat content of gut)

→ Ecology's proposal fails to account for variability in soils (soil chemistry, particle size & characteristics)

→ Bioavailability studies show a wide range of values

→ It is unclear whether available studies reliably depict soil bioavailability

- ***Whether the assumptions used in applying the information to the facility are valid and would ensure the proposed modification would err on behalf of protection of human health and the environment.***

  For establishing cleanup levels for unrestricted land use, residential land use, MTCA defines the reasonable maximum exposure, the highest exposure that is reasonably expected to occur under current and potential future site conditions, in terms of exposures to children. Ecology evaluated the variability in exposure estimates by performing a screening level Monte Carlo analysis using the Crystal Ball software. This involved replacing the point estimates for several input parameters with probability distributions for those values. The analysis indicates that deterministic (point) exposure estimates based on the MTCA exposure parameters and the 0.4 value fall at the upper end of the simulated exposure distribution.

- ***Whether the information adequately addresses populations that are more highly exposed than the population as a whole and are reasonably likely to be present at the site.***

  Method B cleanup levels focus on the protection of children potentially exposed at a site. Board members noted during the October 23rd SAB meeting that increased body fat and dietary habits may influence the soil bioavailability of dioxins/furans. Although Ecology has not identified specific documentation related to soil bioavailability of dioxins/furans for children or due to body fat, there is substantial documentation related to children identified as susceptible populations to increased risks of adverse health effects from exposures to dioxins/furans from maternal body burdens or as nursing infants (NAS, 2003). Several factors have been identified that may increase or decrease the bioavailability of dioxin/furans from soils which may increase or decrease a child's exposure.

Factors that influence soil bioavailability of dioxins/furans include:

→ Soil type (soil chemistry and soil characteristics). High organic content and small soil particle size may reduce the bioavailability of dioxins/furans from soil.

→ Contact time (influence of residence time the contaminants are in contact with the soils). The longer the period of time the dioxins/furans remain in the soil matrix the more influence the soil matrix may have on bioavailability.

→ Contaminant concentrations within the soil. Higher concentrations of soil contaminants may increase the potential for exposure with an increase in bioavailability.

→ Dominant congeners within the soil. Bioavailability may be influenced depending on the dominant congeners in the soil with the hexa-, hepta-, and octa – congeners less bioavailable than the tetra- congeners.

A Washington State reconnaissance study conducted in 1990 to provide information on metal concentrations in soils described different soil types throughout Washington (Ames, 1994). The diversity of soils in Washington State is associated with the variety of parent materials, climates, and topography where the soils were formed. Soils range from a glacial till, beach sands along the Washington coast, to others formed in the forested mountains. After removal of coarse gravel or cobble, some of the soil descriptions used by the U.S. Geological Survey (Water-Resources Investigations Report 95-4018) for the Washington State reconnaissance study included:

→ Brown loamy sand

→ Brown sand

→ Silt loam

→ Brown silty clay

→ Brown gray fine sand

→ Sandy loam

The variability of Washington State soil types, and differences between Washington State soils and the soil types used in the bioavailability studies that are not well characterized makes any comparison or extrapolation between the soils problematic. Differences in soil types found in Washington State and the differences between soils in Washington State and the soils used in the bioavailability studies contributes to the variability and uncertainty regarding the soil bioavailability of dioxins/furans which may increase or decrease potential exposures.

- ***Whether adequate quality assurance and quality control procedures have been used, any significant anomalies are adequately explained, the limitations of the***

information are identified and the known or potential rate of error is acceptable.

Ecology has relied on studies and committee analyses that have been subjected to extensive public and peer review. However, Ecology recognizes the limitations regarding the soil bioavailability studies for dioxins/furans:

- Limited number of studies has been identified;
- Limited soil types have been evaluated for bioavailability;
- Soil types used in the studies have been poorly characterized;
- Difficult to associate soils studies with soils found in Washington State;
- No standard protocol (methodology) has been developed or at least identified to evaluate soil bioavailability;
- Extrapolation to human populations from animal soil bioavailability studies may be problematic; and
- Reported oral bioavailabilities from soil have a large range.

Concluding Remarks

Although no standard protocol or methodology exists to determine the soil bioavailability of dioxins/furans, Ecology relied on peer reviewed technical articles, expert panel reviews (National Academy of Sciences), and EPA's dioxin reassessment to help formulate the proposed rule change to establish a default GI absorption factor of 0.4.

References

Soil Bioavailability Technical Studies

Bonaccorsi et. al., 1984. [Bonaccorsi, A.; di Domenico, A.; Fanelli, R., Merli, F.; Motta, R.; Vanzati, R.; and Zapponi, G.A. (1984) The Influence of Soil Particle Adsorption on 2,3,7,8-Tetrachlorodibenzo-p-dioxin Biological Uptake in the Rabbit. Archives Toxicology, Supplement 7, pages 431-434]

Lucier et. al., 1986. [Lucier, G.W.; Rumbaugh, R.C.; McCoy, Z.; Hass, R.; Harvan, D.; and Albro, P. (1986) Ingestion of Soil Contaminated with 2378-Tetrachlorodibenzo-p-duixub (TCDD) Alters Hepatic Enzyme Activities in Rats. Fundamental and Applied Toxicology, 6, pages 364-371]

McConnell et. al., 1984. [McConnell, E.E.; Lucier, G.W.; Rumbaugh, R.C.; Albro, R.W.; Harvan, D.J.; Hass, J.R.; Harris, M.W. Dioxin in Soil: Bioavailability After Ingestion by Rats and Guinea Pigs. Science. March 09, 1984. Volume 232. Pages 1077 – 1079]

Poiger and Schlatter, 1980. [Poiger, H.; and Schlatter, Ch. (1980) Influence of solvents and Adsorpbents on Dermal and Intestinal Absorption of TCDD. Food and Cosmetics Toxicology, Vol. 18, pages 477-481]

Shu et. al., 1988. [Shu, H.; Paustenback, D.; Murray, F.J.; Marple, L.; Brunck, B. (1988) Bioavailability of Soil-Bound TCDD: Oral Bioavailability in the Rat. Fundamental and Applied Toxicology 10, 648 – 654]

Umbreit et. al., 1986. [Umbreit, T.H.; Hesse, E.J.; and Gallo, M.A. Bioavailability of Dioxin in Soil from a 2,4,5-T Manufacturing Site. Science. April 25, 1986. Volume 232, Number 4749, pages 497-499]

Van den Berg, et. al., 2006. Van den Berg, Martin; Birnbaum, Linda, S., et. al., 2006. The 2005 World Health Organization Reevaluation of Human and Mammalian Toxic Equivalency Factors for Dioxins and Dioxin-Like Compounds. Toxicological Sciences 93(2), 223-241.

EPA References

EPA, 1994 (a). Estimating Exposure to Dioxin – Like Compounds. Volume II: Properties, Sources, Occurrence and Background Exposure. EPA/600/6-88/005Cb. June 1994.

EPA, 1994 (b). Estimating Exposure to Dioxin – Like Compounds. Volume III: Site-Specific Assessment Procedures. EPA/600/6-88/005Cc. June 1994.

Expert Committee References

NAS, 2003. Institute of Medicine of the National Academies. Dioxins and Dioxin-Like Compounds in the Food Supply. Strategies to Decrease Exposure. 2003.

NRC, 2003. National Research Council of the National Academies. Bioavailability of Contaminants in Soils and Sediments. Processes, Tools, and Applications. 2003.

NRC, 2006. National Research Council of the National Academies. Health Risks from Dioxin and Related Compounds. Evaluation of the EPA Reassessment. July 2006.

Schecter and Gasiewicz, 2003. Dioxins and Health, Second Edition. Edited by Arnold Schecter and Thomas A Gasiewicz. Wiley-Interscience (A Jonhn Wiley & Sons, Inc., Publication) Chapters 5 and 6.

Soil References

Ames, 1994. Ames, Kenneth C. Washington State Metals in Soils Program: Preliminary Results. Hydrological Science and Technology, Volume 10, Number 1-4, pages 15-29. 1994.

Ames and Prych, 1995. Ames, Kenneth C. and Prych, Edmund A. 1995. Background Concentrations of Metals in Soils From Selected Regions in the State of Washington. U.S. Geological Survey, Water-Resources Investigations Report 95-4018.

Mean Estimates of Relative Oral Bioavailability of TCDD from Soil

(Based on liver concentrations, unless otherwise noted)

	Author	Animal	Relative Bioavailability	Notes
Times Beach				
	McConnell	Guinea Pig	<48%	1 µg/kg dose
	McConnell	Guinea Pig	19%	3 µg/kg dose (dead animals only)
	Shu	Rat	63% (reported as 43%)	43% from inappropriate adjustment (real range 52-70%)
Minker Stout				
	McConnell	Guinea Pig	<57%	1 µg/kg dose
	McConnell	Guinea Pig	14%	3 µg/kg dose (dead animals only)
	McConnell	Rat	45%	5 µg/kg dose
	McConnell	Rat	49 – 112%	Based on AHH induction
	Lucier	Rat	22 – 45%	Dose range 0.015 – 5.5 µg/kg
	Lucier	Rat	56 - 121%	Based on AHH induction
	Lucier	Rat	65 - 117%	Cytochromes P450 induction
Seveso				
	Bonaccorsi	Rabbit	32%	
Seveso (recontaminated)				
	Bonaccorsi	Rabbit	56 – 71%	
	Poiger	Rat	44 – 66%	
Newark manufacturing				
	Umbreit	Guinea Pig	~0.25%	

Newark salvage	Umbreit	Guinea Pig	24%	

Soil From	Reference	Relative Bioavailability	Endpoint Measured	Animal	Gavage Dose (µg TCDD/kg body weight)	Soil Concentration (µg TCDD/kg soil)	Particle Size	Notes
Times Beach, MO								
	McConnell	<48%	Liver content	Guinea Pig	1.3	770 µg/kg	< 250 µm	Dead animals
		19%	Liver content	Guinea Pig	3.8			
	Shu	62%	Liver content	Rat	0.0032			
		70%	Liver content	Rat	0.007			
		67%	Liver content	Rat	0.04			
		60%	Liver content	Rat	0.037			
		67%	Liver content	Rat	0.175			
		52%	Liver content	Rat	1.45			
Minker Stout, MO								
	McConnell	<57%	Liver content	Guinea Pig	1.1	880 µg/kg	< 250 µm	
		14%	Liver content	Guinea Pig	3.3			Dead animals
		54%	AHH induction	Rat	0.22			
		112%	AHH induction	Rat	0.44			
		49%	AHH induction	Rat	1.1			
		92%	AHH induction	Rat	5.5			
	Lucier	22%	Liver content	Rat	1.1	880 µg/kg	< 250 µm	
		45%	Liver content	Rat	5.5			
		56%	AHH induction	Rat	0.015			
		121%	AHH induction	Rat	0.044			
		113%	AHH induction	Rat	0.1			
		81%	AHH induction	Rat	0.22			
		103%	AHH induction	Rat	0.5			
		60%	AHH induction	Rat	1.1			
		61%	AHH induction	Rat	2.0			

		106%	AHH induction	Rat	5.5			
		117%	P450 induction	Rat	0.015			
		91%	P450 induction	Rat	0.044			
		90%	P450 induction	Rat	0.1			
		76%	P450 induction	Rat	0.22			
		105%	P450 induction	Rat	0.5			
		65%	P450 induction	Rat	1.1			
		71%	P450 induction	Rat	2.0			
		84%	P450 induction	Rat	5.5			
Seveso, Italy								
	Bonaccorsi	32%	Liver content	Rabbit	0.56	81 µg/kg	30-74 µm	7 x 80 ng/kg doses
Seveso								
(recontaminated)	Bonaccorsi	71%	Liver content	Rabbit	0.28	30 day soil contact		7 x 40 ng/kg doses
		56%	Liver content	Rabbit	0.56	30 day soil contact		7 x 80 ng/kg doses
	Poiger	66%	Liver content	Rat	0.11	15 hour soil contact		
		44%	Liver content	Rat	0.11	8 hour soil contact		
Newark mfg site								
	Umbreit	~0.25%	Liver content	Guinea Pig	12	Mghing site:1500 to 2500 ppb; Salvage yard: ~180 ppb	For both sites: medium dense, black, coarse to fine-grained sand fill with some medium to fine gravel, traces of silt, organic matter & cinders	
Newark salvage site								
	Umbreit	24%	Liver content	Guinea Pig	0.32			

Observations Made by [EPA, 1994 (a)] Regarding 2, 3, 7, 8 - TCDD Bioavailability Studies	
Documentation	**Observation**
McConnell et. al., 1984	For Times Beach Soil → LD 50 data indicate TCDD in soil ~25% as toxic as in corn oil. → Comparing animal dying early, liver retention of TCDD in soil group ~50% of that in corn oil vehicle group. → Comparing animal surviving experiment, liver retention of TCDD in soil group ~20% of that in corn oil vehicle. For Minker Site Soil → LD 50 data indicate TCDD in soil ~30% as toxic as in corn oil. → Comparing animals dying early, liver retention ~50% of that in corn oil group → Comparing animal surviving experiment, liver retention of TCDD in soil group ~25% of that in corn oil vehicle.
McConnell et. al., 1984 and Lucier et. al., 1986	For Minker Site Soil → Introduction of AHH and UDP glucuronuyltransferase activity > 50% of that in groups receiving TCDD in corn oil → Liver retention 20-40% of that in rats receiving equal dose of TCDD in corn oil.
Bonaccorsi et. al., 1984	TCDD 30% as bioavailable from soil as from solvent vehicle
Poiger & Schlatter,1980	→ Liver retention ~ 40-70% of that in ethanol vehicle groups → <0.1% retention in liver with TCDD on activated carbon
Umbreit et. al., 1986	For Newark Manufacturing Site → TCDD in soil had retention in liver ~1% as great as with salvage site soil

	For Newark Salvage Site → Liver retention similar to TCDD in corn oil from McConnell study (56%)